(*b*) THE PATHOLOGICAL CHANGES IN THE NEURONE IN NERVOUS DISEASE.[1]

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In discussing the pathological changes in the neurone in nervous disease the most important question we have to answer is: Does pathology afford any support for the neurone doctrine—*i. e.*, are the changes that occur in disease of the nervous system of such a character that we may obtain from them evidence of the existence of neurones?

To answer this question it must be shown whether degenerative processes have a tendency to affect distinct groups of nerve cells, including their dendritic processes, axones, collaterals and terminal ramifications, to the partial or complete exclusion of other groups.

It must be shown whether the neurone in its entirety, either motor or sentory, is affected by disease—*i. e.*, whether the cell-body may become diseased and die without disease and death of the axone, or whether the axone may suffer or perish without destruction or involvement of the cell-body.

It must be shown whether a morbid process is always limited to a central or peripheral neurone, or whether degeneration passes from one to the other, from a motor to a motor neurone, or from a sensory to a sensory neurone, without any interference at the parts that have been regarded as points of contact of the neurones. It must be shown whether disease of a sensory neurone affects a motor neurone, or *vice versa*. To put the whole matter in a few words, we must obtain from pathology the evidence that what we recognize as a neurone suffers when diseased in so peculiar a manner that we may recognize in this involvement the individuality of the structure.

I shall not give a résumé of the pathology of the cell-body; that has been well done by capable investigators—van Gehuchten, Marinesco, Ewing, Barbacci, Robertson and others; but I shall endeavor to apply some of the literature on the subject and the results of my own investigations to the solution of the problems I have mentioned.

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[1] From the William Pepper Clinical Laboratory (Phœbe A. Hearst Foundation). Read at the twenty-sixth annual meeting of the American Neurological Association, May 1, 2, and 3, 1900.

We cannot deny that degeneration has a very evident tendency to involve distinct groups of nerve-cells, including their various processes. The existence of systemic diseases and of combined systemic diseases admits of little dispute, and we have in this limitation of morbid processes one argument in favor of neurones. Tabes, amyotrophic lateral sclerosis, Friedreich's ataxia and other diseases might be mentioned in illustration. It is not because all the axones affected in these diseases conduct impulses in one direction that they degenerate. We have in tabes, for example, a degeneration of posterior root fibers, including in some cases the descending roots of certain cranial nerves that are similar to the posterior roots of the spinal cord—the sensory fifth and the combined root of the ninth and tenth nerves—as I have seen in four or five cases. We do not have as a common finding in tabes degeneration of other ascending tracts; of the direct cerebellar or of the fillet. We have a selective degeneration of the primary sensory neurones, and a degeneration that does not as a rule pass to sensory neurones of another system. We have manifested in the pathological changes of certain systems an evidence of an individuality of these systems. I shall not dwell on this aspect of the subject lest I infringe on Dr. Sachs' rights.

We may inquire to what degree a neurone in its entirety becomes diseased. If we cut an axone, either central or peripheral, we know from the investigations of Nissl, Marinesco, van Gehuchten and many others that the cell-body in which this axone arises undergoes rapid alteration and possibly death, and that this alteration is probably more intense the nearer to the cell-body the division of the axone is made. Not only is the cell-body affected, but the central portion of the axone may also suffer more or less alteration. I need not refer to the degeneration of the peripheral end; that is well recognized as the degeneration of Waller. The earlier in the life of the animal the injury to the axone occurs the greater is the atrophy of the cell-body in which the axone arises. In a case of Pott's disease that I[2] studied the compression in the cervico-thoracic region probably began at the third year of the child's life, and by the eighth year the direct cerebellar tract *below* the compression and the cell-bodies in the column of Clarke had disappeared. I attach much importance to these findings, as I believe that mine was the first case recorded of complete atrophy of the cells of Clarke's column from a cervico-thoracic lesion.

Barker[3] in 1897 found *chromatolysis* in the cell-bodies of Clarke's columns in epidemic cerebrospinal meningitis, and explained it as a "reaction at distance."

Sano[4] in July, 1897, described *chromatolysis* of the cell-bodies of the column of Clarke, resulting from the pressure of a tumor on the direct cerebellar tract, the compression being chiefly at the fourth cervical segment. The alteration in Clarke's column consisted of central chromatolysis and some deformity of the nucleus. From the study of this case Sano concluded that the law of reaction at distance in a cell-body as a result of injury to its axone exists as truly for the central neurones as for the peripheral.

In my paper read in January, 1898, at the Johns Hopkins Hospital and published in June, 1898, I described complete destruction of the cell-bodies in Clarke's columns, and not merely chromatolysis, from a cervico-thoracic lesion.

Van Gehuchten[5] also has observed chromatolysis of these cell-bodies after the division of the spinal cord in the dog.

Sano,[6] in a later paper, reported the finding of chromatolysis in Clarke's column in six cases, resulting from lesions of the direct cerebellar tract.

I have become somewhat skeptical as to the value of chromatolysis in Clarke's column, and am inclined to think that these cells are especially liable to react in this way from many causes.

The change in the central end of the motor axone, apart from chromatolysis, after division of the axone has occurred, is not rapid, especially when the injury is at some distance from the cell-body. I have observed retrograde atrophy of the pyramidal fibers in several instances, but only when the transverse lesions were of long duration.

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[2] Spiller, The Johns Hopkins Hospital Bulletin, No. 87, June, 1898.
[3] Barker, Brit. Med. Journal, 1897, Vol. II, p. 1839.
[4] Sano, Journal de Neurologie, July 20, 1897, p. 276.
[5] Van Gehuchten, Journal de Neurologie, June 5, 1898, p. 238.
[6] Sano, Journal de Neurologie, Aug. 5, 1898, p. 313.

I have studied a case of peripheral nerve degeneration, the symptoms of which had existed for at least five or six years.

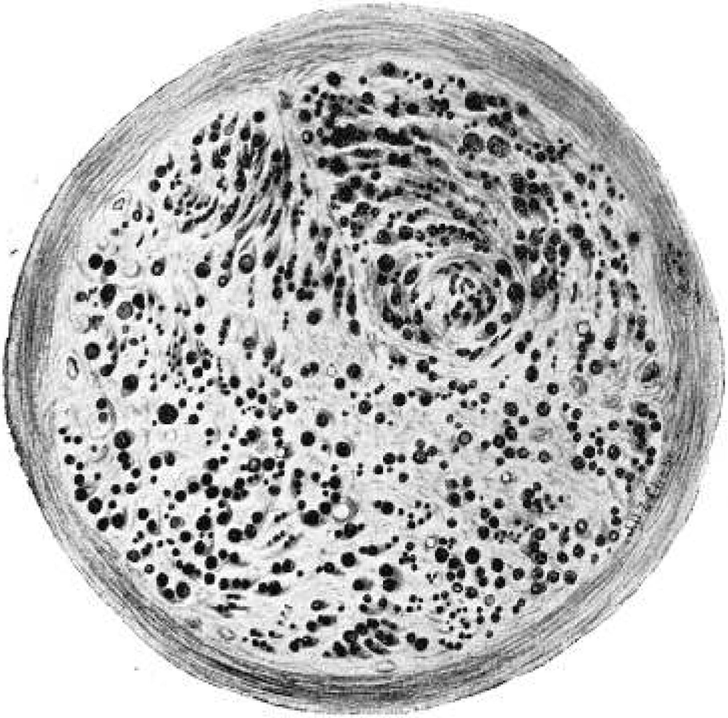

Fig I. Case of chronic neuritis of five or six years' duration. Nerve fibers of the left internal plantar nerve showing much degeneration. Some of the cell-bodies, from which the axones of this nerve arise, show the "reaction at distance" in the form of central chromatolysis and displacement of the nucleus.

The terminal portions of some of the branches from the sciatic show very distinct degeneration of the nerve fibers and overgrowth of the connective tissue in and about the nerve bundles. (Fig. I.). Many of the cell-bodies of the anterior horns of the lumbar region present central chromatolysis and displacement of the nuclei (Fig. II.), and this is in a case of chronic neuritis.

Nissl's stain is, of course, the most valuable for the study of nerve cells, but pronounced degeneration may often be told by the ammonium carmine stain. In my case of Pott's disease, to which I have referred, and in a case of acute poliomyelitis in an adult,[7] the destruction of cell-bodies was most evident by the carmine stain, and I am somewhat skeptical as to the importance of cellular changes that have existed many years, and cannot at all be detected by the carmine stain.

It seems that in acute diseases involving the axone, the cell-body in which the axone arises suffers, but if the disease becomes chronic, and is in the distal part of the axone, the cell-body may not show any serious alteration, even by Nissl's stain. The neurone as a whole suffers, but the chromatolysis may disappear, unless the degeneration involves a portion of the axone too near the cell-body. Dejerine and Thomas,[8] in a case of neuritis, found the nerves greatly altered without any appreciable change by the Nissl method in the cell-bodies in

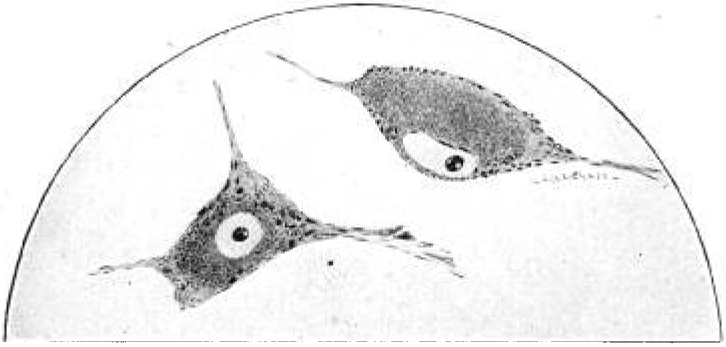

Fig. II. Chronic neuritis of five or six years' duration. The cell-bodies in the anterior horns in the lumbar region show the "reaction at distance."

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[7] Sherman and Spiller, The Philadelphia Medical Journal, March 31, 1900.

[8] Dejerine and Thomas, Comptes rendus de la Soc. de Biologie. 1897.

which these fibers arose. Cellular alteration, possibly, had occurred in this case, and the cell-bodies had recovered. The importance of chromatolysis is disputed. To Dejerine and Thomas it has little value, but to Schaffer it is an index of degeneration of a more essential portion of the cytoplasm. Dejerine[9] showed in 1889, by the examination of nine cases of tabetic muscular atrophy, that the peripheral nerves in their terminal portions were much diseased, and yet no cellular changes were found in the spinal cord. The Nissl method, of course, was not employed. If chromatolysis occurred in the cell-bodies in these cases—as it did occur in my case of chronic neuritis, the material from which I received from Dr. Mills; and in a case of facial paralysis of six months duration, now reported by Dr. Mills and myself (Fig. III.)—it had at least not led to atrophy of the cell-bodies.

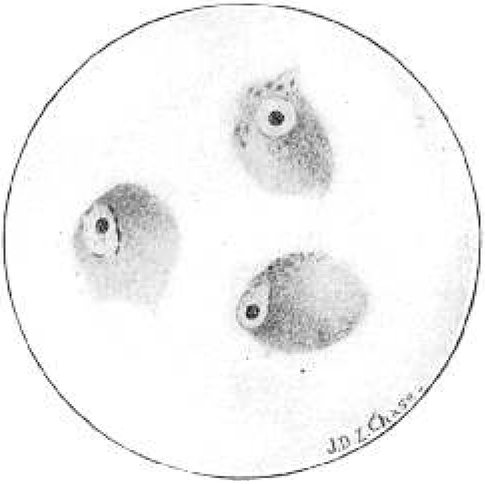

Fig. III. Cell-bodies of the facial nucleus in a case of peripheral facial palsy of six months' duration. A few of the cell-bodies within the nucleus are in a condition of almost complete chromatolysis, with displacement of the nucleus.

Van Gehuchten[10] holds that the restoration of a cell-body from chromatolysis occurring after division of the axone, is not dependent upon the reunion of the axone, and he refers to a similar statement made by Nissl. Van Gehuchten believes that reunion of the axone is without effect upon the restoration of the chromophilic bodies, but if restoration of the axone does not occur, the cell-body finally atrophies and disappears. Marinesco[11] advances somewhat different views. According to him the reparative process in a cell-body after its axone is cut is dependent upon the reunion of the axone, although both Marinesco and van Gehuchten seem to be in accord as to the final atrophy of the cell-body when the two ends of the axone remain ununited. Simple chromatolysis seems to me to be of doubtful value as indicative of cellular degeneration if, as van Gehuchten believes, it disappears, although the cell may die later, and is only a temporary reaction of the cell-body after division of its axone. Van Gehuchten has been unable to obtain even temporary chromatolysis in the spinal cell-bodies of rabbits and dogs by cutting the axones of these cell-bodies, but with de Buck,[12] he has found chromatolysis in the spinal cord of man after amputation of a limb. Chromatolysis in man after amputation of a limb has been observed also by Flatau[13] and by Sano.[14] I have had the rare good fortune to obtain the spinal cord from a case in which amputation at the hip joint was followed by death after five and a half days. The cell-bodies in the lumbo-sacral region on the side of the amputation have undergone great chromatolysis, and in some of the cell-bodies displacement of the nucleus has occurred. The cell-bodies in the anterior horn of this side stain very faintly. On the other side of the cord the cell-bodies of the anterior horn are much more deeply stained, although some of them show chromatolysis. The difference in the condition of the cell-bodies of the two horns is striking. The chromatolysis in many cell-bodies is complete; in others, it is merely central.

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[9] Dejerine, "Sur l'atrophie musculaire des ataxiques," 1889.

[10] Van Gehuchten, "Anatomie du système nerveux de l'homme," third edition, Vol. 1, 1900, and Presse méd., 1899, p. 3.

The neurone in all its parts is not always promptly affected when the cell-body is seriously diseased. The case of acute poliomyelitis reported by Dr. Sherman and myself (*l. c.*), is an evidence of this. The disease was of short duration, but was sufficiently long to cause destruction of the cell-bodies of the anterior horns, and to leave the motor roots unaffected, not even causing swelling of the axones. I could refer to a number of similar cases in literature. In the case of hemorrhagic pachymeningitis reported to this Association last year by Dr. McCarthy and myself,[15] intense alteration of the cell-bodies was observed, but none of the axones. If the objection should be raised that this cellular change was recent, and possibly from edema; and therefore alteration of the axones had not time to develop, I would reply that precisely the same changes were observed by Hirsch,[16] in a case of amaurotic family iodiocy, and that this observation by Hirsch and the improbability of an edema of *recent* origin in our case, would lead me to believe that the cellular changes throughout the central nervous system probably were not recent. The changes in Hirsch's case could not have been of post-mortem origin, as the necropsy was made four hours after death. In his case, however, the change in the cell-bodies was associated with degeneration of the pyramidal tracts, and in ours it was not. I have recently studied another case in which the same cellular changes existed, and degeneration of the pyramidal tracts did not occur. This was a case with the symptoms of meningitis in a feeble-minded child. Cellular changes such as those just described I have been unable to find in cortical edema.

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[11] Marinesco, Presse méd., 1898, pp. 201-206.
[12] Van Gehuchten and de Buck, Journal de Neurologie, 1898, p. 94.
[13] Flatau, Deutsche med. Wochenschrift, 1897, p. 278.
[14] Sano, Journal de Neurologie, 1897.

It would seem, therefore, that the cell-body, though greatly altered morphologically, is still capable of exerting an influence on the health of the axone, and that so long as the cell-body persists and is not too seriously altered, the axone may live. An axone is only partially dependent upon the cell-body for its vitality, and if the blood supply to it at a considerable distance from the cell-body is cut off, that portion deprived of the circulation dies, but the cell-body seems to be necessary to the axone to enable it to appropriate the nourishment brought to it.

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[15] Spiller and McCarthy, THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1899, p. 677.

[16] Hirsch, THE JOURNAL OF NERVOUS AND MENTAL DISEASE, 1898, p. 538.

Diseases that are due to poisons also have a decided tendency to affect certain neurones in their entirety, as was evident in the case of Landry's paralysis reported by Dr. Mills and myself,[17] in which only the peripheral motor neurones were affected. Similar cases are reported in literature.

Central motor neurones degenerate in a manner very like that of the peripheral motor neurones. Marinesco[18] found very intense alteration of the cells of Betz, and only of these cells, in the paracentral lobule, following a lesion of the internal capsule. These large cell-bodies may entirely disappear, as the result of such a lesion. The cellular changes consist of tumefaction of the cell-body, chromatolysis and alteration and displacement of the nucleus. Marinesco thus confirms the statement of v. Monakow,[19] that the large pyramidal cell-bodies of the paracentral lobule disappear after destruction of the internal capsule. From the integrity of the other cell-bodies of the paracentral lobule, Marinesco seems to conclude that these smaller cell-bodies do not give origin to motor fibers. His words in speaking of the cells of Betz are: "Ce sont ces cellules qui donnent naissance aux fibres pyramidales." As the large cells of Betz are scarce in the lower portions of the motor cortex, we may hesitate to accept the view that Betz's cells are the only ones in the motor cortex that are motor in function. Marinesco refers to the fact that Dotto and Pusateri have seen cellular changes in the motor cortex following destruction of the internal capsule.

Ballet and Faure[20] found that after the fibers of projection from the motor area were cut, the motor cortical cell-bodies atrophied. The cellular changes were similar to those that occur in the motor cell-bodies of the cord when the peripheral motor fibers are divided. They expetimented on seven dogs, and presumably made the division of the fibers not far below the cortex. The point of attack is of importance in the production of cellular lesions, as the nearer the interruption of the axone is to the cell-body, the greater is the alteration of the cell-body.

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[17] Mills and Spiller, The Journal of Nervous and Mental Disease, 1899.

[18] Marinesco, Revue neurologique, 1899, p. 358.

[19] Von Monakow, "Gehirnpathologie," p. 118.

[20] Ballet and Faure, Semaine méd., 1899, p. 109.

I have studied the paracentral lobule in five cases of capsular lesion, three of which were due to hemorrhage of various durations, but I have been unable to convince myself that characteristic changes occurred in the cells of Betz. I have been more fortunate in my examination of the cortex in cases of long duration. One of the brains studied was from a half-grown boy who had survived for ten or eleven years the closure of the left Sylvian artery. The motor area was destroyed except in its extreme upper portion. The motor axones from this area were cut near their origin. Very few cell-bodies were found in the paracentral lobule, and the cells of Betz were almost entirely absent. The sections from the paracentral lobule of this brain were exceedingly interesting in comparison with those from the paracentral lobule of a brain in which the lower part of the left motor area was destroyed by porencephaly. The motor axones above this lesion were not injured so close to the cell-bodies. The porencephaly naturally suggests a congenital lesion, and the motor axones from the upper left motor area were probably arrested in their downward growth. The results were similar to those produced by dividing the axones. As the lesion was not so near the cell-bodies of origin in the paracentral lobule as in the former case, fewer cell-bodies had disappeared entirely, and yet those present were much below the normal number, were small and rounded, the pericellular spaces were large, and the cells of Betz seemed to be absent. These two cases have given results very like those obtained experimentally by Ballet and Faure, only the cellular changes in my cases were much more intense. Destruction of the cells of Betz from cerebral lesions have been observed not only by v. Monakow, but also by Moeli, Henschen, and Mahaim.

The peripheral sensory neurone reacts in a peculiar way to traumatism. It is very remarkable that, while division of the peripheral process of a spinal ganglion cell-body causes very distinct degeneration of this cell-body (Lugaro, Mering, Fleming, van Gehuchten, Cassirer), and even complete destruction of the cell-body according to some, division of the central process causes no cellular reaction. This is a very interesting statement and of much value in the explanation of tabes. Marinesco [21] denies that the cell-body of the peripheral sensory neurone dies when its peripheral process is cut, as van Gehuchten believes.[22]

Cassirer[23] has found that after a peripheral nerve is cut a large number of cell-bodies in the spinal ganglion belonging to this nerve degenerate, but only a few are so greatly altered that they probably undergo complete destruction. As a result of this cellular degeneration he finds that a moderate degeneration of posterior roots occurs. The changes which Cassirer found in the posterior roots as a result of the division of the peripheral nerve were slight, as they were also in some similar experiments performed by Redlich, and therefore Cassirer thinks his findings afford no support for the theory that tabes begins in the peripheral nerves. There is no comparison, he thinks, between the slight degeneration of the posterior roots when a whole nerve is cut and the intense degeneration of these roots in tabes.

In a Gasserian ganglion removed recently by Dr. Harvey Cushing for trifacial neuralgia I found alteration by Nissl's stain in quite a number of the cell-bodies of the ganglion—by no means the majority, however—but was not able to detect any change in the sensory root, although I found alteration of the sensory root in another ganglion removed by Dr. Cushing. Krause[24] also reports disease of a sensory root. My examination of the ganglion referred to and of its sensory root has given results similar to those obtained by Cassirer and Redlich in experiments on the spinal ganglia, *i. e.,* alteration of cell-bodies of the ganglion with little alteration of the cellulifugal processes.

The destruction of the spinal ganglion was very much less in Cassirer's experiments than in those of Lugaro and van Gehuchten, and therefore we might expect slight alteration of the posterior roots in Cassirer's cases. It seems impossible to examine a picture in which the cells are as few in number as in that given by van Gehuchten[25] on p. 335 of the recent edition of his text book, and to believe that the cellulifugal processes of the cell-bodies of the ganglion in such a case were only slightly degenerated.

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[21] Marinesco, Presse méd., 1898, p. 201.

[22] Van Gehucten, "Anatomie du système nerveux de l'homme," third edition, Vol. 1, 1900.

[23] Cassirer, Deutsche Zeitschrift für Nervenheilkunde, Vol. 14, p. 150.

[24] Krause, "Die Neuralgie des Trigeminus," Leipzig, 1896.

Schaffer's[26] finding of normal cell-bodies by the Nissl method in the spinal ganglia in tabes is a further proof that the cell-bodies of the spinal ganglia do not react promptly to lesions of their central processes. I also in the examination of a case of tabes by Nissl's stain have found the cell-bodies in the spinal ganglia of the lumbar region normal.

We see, therefore, that on the whole there is a tendency for the entire neurone to undergo alteration when it is attacked by disease or injured experimentally, but that a portion may be more resistant than the rest and may recover even though at first affected, although the end in union with the cell-body may finally atrophy. The earlier in life the lesion occurs the less is the resistance of the neurone. From these facts we have some evidence of the individuality of the neurone.

A very interesting question is in regard to the degree of limitation of degeneration to one set of neurones, either sensory or motor. It is quite certain that a restriction exists, but occasionally this restriction is overcome. Tertiary degeneration —and by that I mean a degeneration in another series of neurones resulting from secondary degeneration of a series of neurones nearer the origin of the impulses—does not seem to be of very frequent occurrence. It is important to make a distinction in regard to this matter. The changes that occur in a second neurone associated with *primary* degeneration in a first neurone—and by that I mean degeneration not due to a focal lesion—cannot be compared with the degeneration of one neurone following degeneration of another from a focal lesion. In the first instance we have reason to believe that the first neurone that undergoes primary degeneration does so as a result of imperfect development, or possibly as the result of the action of a poison, and we do not know that the same causes have not produced the degeneration of the second neurone. In amyotrophic lateral sclerosis, for example, of which I have studied the specimens of two cases, we have no proof that the degeneration of the peripheral motor neurones is the result of degeneration of the central motor neurones, or *vice versa.*

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[25] Van Gehucten, "Anatomie du système nerveux," third edition, Vol. I.

[26] Schaffer, Neurologisches Centralblatt, 1398, p. 2.

I have examined cases of hemiplegia in the adult with sclerosis of the pyramidal tract, but have never seen degeneration of the cell-bodies of the anterior horns by the carmine stain and of the nerve fibers arising from them, *i. e.,* I have not found tertiary degeneration in these cases. In my case of Pott's disease of early development, to which I have referred, in which both pyramidal tracts were destroyed, the cell-bodies in the anterior horns in the lumbar region by the carmine stain were normal in shape and size, the dendritic processes were not entirely perfect, the nuclei were central and the cells were normal in number. This was an excellent case for the study of tertiary degeneration, as the lesion occurred at the third year of life, and the cell-bodies of Clarke's column had disappeared as a result of retrograde atrophy, but tertiary degeneration if it existed had not caused much alteration.

I have examined by the carmine stain a case of spinal hemiplegia from a lesion in the cervical region which had existed for a number of years. The cell-bodies in the lumbar region on the side of the degenerated crossed pyramidal tract were numerous, the nuclei were central, but the dendritic processes were possibly not perfectly developed.

Of course the cells in both these cases might have shown some alteration if Nissl's method had been employed, but I chose two cases of lesion of the lateral columns in the cervical region to show that atrophy of the cell-bodies of the anterior horns detectable by carmine does not occur to any extent from degeneration of the lateral columns. Possibly a lesion developing even earlier than the third year of life might give different results, or I might have obtained chromatolysis by Nissl's method in these cases. I have recently obtained a spinal cord which was greatly compressed in the upper cervical region by an intradural tumor. The patient had been paralyzed in all the extremities. Many of the cell-bodies in the anterior horns of the lower cervical region are much diseased and are in a condition of central chromatolysis and vacuolation with displacements of the nucleus (Fig. IV.). In the lumbar region the altered cell-bodies are much less numerous. This is possibly tertiary degeneration, but some of it may be "reaction at distance" from the injury of the axones of cells located lower in the cord.

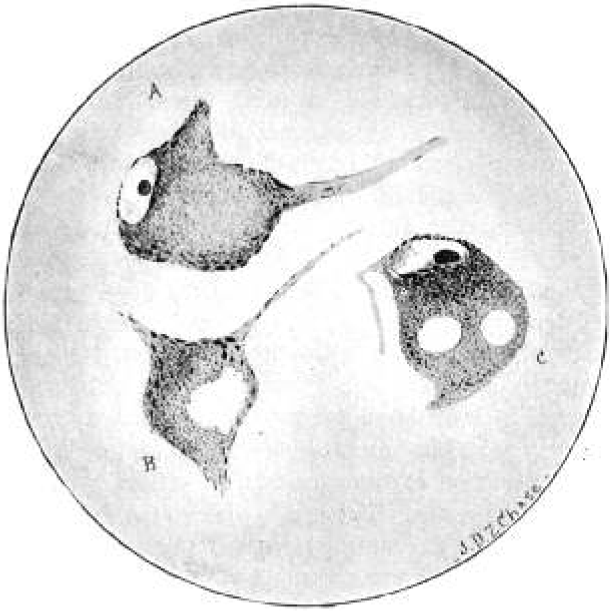

Fig. IV. Cell-bodies of the anterior horns in a case of tumor of the upper cervical region. Many of the cells show central chromatolysis and vacuolation. Cell-body A is from the lumbar region, B and C from the lower cervical. The cellular changes may be "reaction at distance" from injury of the axone, or may be tertiary degeneration of the peripheral motor neurone.

I am at present studying a case of very great value—one of cerebral diplegia from an unilateral lesion. The history is imperfect, but it is positively asserted by thoroughly reliable persons that four and a half years before the boy's death he had been able to walk, but his gait was probably not normal.

He soon lost this power after he came under observation, and his limbs became helpless and contractured. I found intense internal hydrocephalus limited to the right hemisphere, and this hemisphere was a thin-walled sac. The motor fibers were greatly injured and the left crossed pyramidal tract was sclerotic, and yet the cell-bodies in the anterior horns of the cervical and lumbar regions seemed to be normal in number, and little change could be detected by Nissl's method. The boy was fourteen years old when he died. Surely this was a very suitable case for testing tertiary degeneration in the peripheral motor neurones.

Schaffer,[27] however, has observed chromatolysis of the spinal motor cell-bodies in recent hemiplegia, and this chromatolysis was especially noticeable in the postero-lateral group. Quite different are the results obtained by Marinesco.[28] In sixteen cases of hemiplegia with degeneration of the pyramidal tract, that he examined, he found alteration of the cell-bodies in the anterior horns of the cord only in three, and in two of these cases the altered cell-bodies were not numerous and might easily have escaped detection. In the case in which the changes were distinct they were like those seen when an axone is cut, and were suggestive of neuritis.

We should be exceedingly cautious in accepting diminution in the size of one anterior horn as a result of degeneration of the pyramidal tract. In the case of malaria of the central nervous system, the report of which I present at this meeting, a slight sclerosis existed in one crossed pyramidal tract and the anterior horn on that side throughout the cord was distinctly smaller than the horn of the other side. The number of the cell-bodies was about the same on the two sides. The sclerosis, was so slight and the symptoms it caused so transient, that I look upon the diminution in size of the anterior horn occurring with the slight sclerosis of the motor tract merely as a coincidence.

Berger[29] has found very distinct degeneration of the cell-bodies of the anterior horns in paretic dementia. This degeneration might have been regarded as due to toxic causes or to degeneration of the pyramidal tracts. The experiments Berger performed are of much interest in the light of Warrington's[30] positive findings. Berger was unable to produce in the dog degeneration of the contralateral anterior horn cell-bodies by destruction of the motor cortex, although the pyramidal tract in the cord was degenerated. In another dog he destroyed the cortical motor area and divided the contralateral posterior roots and allowed the animal to live four weeks. The cell-bodies of the anterior horns were not degenerated. In a cat in which the pyramidal tract of one side had been destroyed for two years no cellular changes in the corresponding anterior horn were found. Dr. McCarthy, at my request, has kindly cut for me posterior roots in three cats. One cat was allowed to live seven days, another nineteen days, and the third twenty days. The examination of the spinal cord from these animals has given results similar to those obtained by Berger. I find no distinct alterations of the cells of the anterior horns resulting from division of the posterior roots.

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[27] Schaffer, Monatsschrift für Psychiatrie und Neurologie, Voi. 2, No. 1.

[28] Marinesco, Semaine méd., 1898, p. 465.

[29] Berger, Monatsschrift für Psychiatrie und Neurologie, Vol. 3, p. 1.

The results of these experiments cannot be applied equally well to man. The dog and cat seldom use one limb separately, and probably all four limbs are innervated from both sides of the brain more nearly equally than they are in man. To cut off the stimulation from the cortex in the dog it would be necessary to destroy both motor tracts, and possibly even then this would not be sufficient on account of the existence of "extra-pyramidal" tracts.

I have re-examined the sections in the case of syringomyelia reported by Dr. Dercum and myself[31] before this Association four years ago. The posterior horn of the right side was destroyed from the first thoracic segment throughout the cervical region, and in the lower part of the cervical region the crossed pyramidal tract on the side of the destroyed posterior horn exhibited distinct retrograde atrophy. The lesions had existed for a number of years and the cells of the right anterior horn had been deprived of all stimulation through the right posterior cervical roots, and to some extent of the stimulation from the brain through the right motor tract of the cord, on account of the retrograde atrophy of the right crossed pyramidal tract. There may possibly be a slight decrease in the number of cell-bodies in the right anterior horn, but this decrease is questionable and the cell-bodies present appear to be normal by the carmine stain, and have well-developed dendritic processes and central nuclei. The case does not give any positive evidence of degeneration of the cell-bodies of the anterior horn from lesions of the posterior roots.

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[30] Warrington. Journal of Physiology, Vol. XXIII.

[31] Dercum and Spiller, The American Journal of the Med. Sciences, 1896.

Degeneration of the peripheral motor neurone certainly may exist at least many years without degeneration of the central motor neurone. I refer in proof of this statement to the interesting and much cited case reported by Senator. The symptoms of amyotrophic lateral sclerosis existed for about five years, and Senator[32] found a pronounced simple, non-inflammatory atrophy of the cell-bodies in the anterior horns of the cervical and thoracic regions. The anterior roots were not distinctly diseased. He says positively that lateral sclerosis was *entirely* wanting.

Dejerine's[33] cases are further proof in this respect. In two cases of progressive spinal muscular atrophy the peripheral motor neurones were intensely diseased, but absolutely no degeneration of the pyramidal tracts was detectable. One case lasted eighteen years and the other ten years. These specimens Dr. Dejerine has permitted me to study. Similar cases have been reported by Dreschfeld, Oppenheim, Nonne, Dutil and Charcot.

I have never seen involvement of the lemniscus as a result of degeneration of the posterior columns. Two cases in literature in which this was reported occur to me. One was a case reported by Schaffer[34] and is of most difficult interpretation; the other is by Rossolimo.[35] In the latter the portion of medulla oblongata containing the nuclei of the posterior columns was not examined, and these nuclei may have been altered independently of the degeneration of the posterior columns. I have traced intense degeneration by Marchi's method from the sacral cord to the nuclei of the posterior columns, but never beyond.

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[32] Senator, Deutsche med. Wochenschrift, No. 20, 1894, p. 433.
[33] Dejerine, Comptes rendus de la Soc. de Biologie, 1895, p. 183.
[34] Schaffer, Archiv für mik. anatomie, Vol. XLIII.
[35] Rossolimo, Archiv für Psychiatrie, Vol. XXI.

Schaffer[36] thinks that the degeneration of the direct cerebellar tract in tabes is an example of the influence of peripheral sensory neurones on central sensory neurones. I know such cases have been reported, but I have never been fortunate enough to observe any, although I have examined many cords from tabetic persons. I think, therefore, that this degeneration must be rare. Schaffer, however, can give no example of the influence of a central sensory neurone upon a peripheral sensory neurone. He has found central chromatolysis and displacement of the nuclei in the cell-bodies of the anterior horns in tabes and he attributes these cellular changes to the degeneration of the sensory roots. The changes, however, may be due to the peripheral neuritis occuring in tabes. I also have seen this chromatolysis of the cells of the anterior horns in tabes.

A statement made by van Gehuchten is of no value as evidence of tertiary degeneration. Van Gehuchten[37] observed chromatolysis of the terminal nucleus of the acoustic nerve after division of the nerve, and reported this finding at the meeting of the Congress in Moscow. He explained this chromatolysis by the theory of Marinesco and regarded it as the result of injury of the first neurone and of loss of irritation normally conveyed by this neurone. Further researches convinced him that his technique was at fault. The view he now holds is that division or injury of a peripheral sensory nerve does not cause early changes in the cell-bodies forming the terminal nucleus of this nerve. He has not, therefore, seen chromatolysis in the terminal nucleus as a result of injury to the peripheral sensory neurone.

I know of no positive evidence that disease of a sensory neurone ever results from disease of a motor neurone.

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[36] Schaffer, Monatsschrift für Psychiatrie und Neurologie, Vol. 3, p. 64.

[37] Van Gehuchten, Journal de Neurologie, Nec. 20, 1898, p. 502.

I am, of course, well aware of Marinesco's[38] views. He teaches that every disturbance of function in a neurone affects the function of the neurone with which it is in connection. Lesion of a sensory neurone causes in course of time alteration of a second sensory neurone of a different series, possibly even of a sensory neurone of a third series. Lesion of the cortical substance causes similar neuronic atrophies, but in an opposite direction. This theory sounds so plausible that we cannot reject it, but my researches cause me to believe that the influence of one neurone upon another has been to some extent exaggerated.

I would not give the impression that tertiary atrophy—I use the word atrophy and not degeneration—does not occur. I believe that when the function of a neurone is destroyed early in life, even though the neurone is not directly injured as, for example, by division of its axone, this neurone whose function has been arrested develops very imperfectly or possibly even atrophies. The diminution in the size of the lateral column following amputation of a limb is regarded as an evidence of this, and I have seen slight diminution of the antero-lateral column following early amputation. Tertiary degeneration in the adult—possibly it is never more than atrophy—I believe to be rare, especially in the motor system. Tertiary atrophy is possibly more common in the sensory system or in the visual tract, and possibly the explanation of this difference lies in the fact that the peripheral motor neurones are under the stimulation of both the pyramidal tracts and of the sensory roots.

The fact that two neurones in connection with one another do not degenerate to the same degree and with the same rapidity from one lesion is evidence that there is some difference in structure at the point where they come together, and that the essential elements of one neurone are not the same essential elements of another neurone.

That degeneration may occasionally pass from one neurone to another is no proof that neurones do not exist. It is certainly not common for systemic diseases to spread irregularly to neighboring areas. The views of Held, Apáthy, Bethe and Nissl may force us to modify our conceptions of the neurone, but the evidence offered by pathology of the existence of neurones, *i. e.*, of structures having a functional individuality, will have to be harmonized with the results of anatomical studies.

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[38] Marinesco, Presse méd., 1898, p. 201.